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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,897	07/05/2005	Manne Satyanarayana Reddy	BULK 3.3-017 U.S.	1563

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EXAMINER	
HAVLIN, ROBERT H	
ART UNIT	PAPER NUMBER
1609	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,897	REDDY ET AL.	
	Examiner	Art Unit	
	Robert Havlin	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,27-30 and 36-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,27-30 and 36-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24, 27-30, and 36-47 are currently pending.

Priority

This application does not contain a proper claim of priority, therefore the prior art date is the actual US filing date of 12/03/2004. The priority documents were not of record.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-7, 13-20, 29-30, 42-44, 47, and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Oxford et al. (US 5,037,845).

The claims recite a product referred to as "A crystalline Form" (-I and -II) of sumatriptan succinate, and the intrinsic experimental data including X-ray powder diffraction, differential scanning calorimetry (DSC), and infra red (IR) in addition compositions thereof, the same product at varying degrees of purity, and "A crystalline form of sumatriptan base" at varying degrees of purity. In addition, the claims are drawn to methods of using the products for treating migraine. Claim 47 is interpreted as a product by process for producing a solid form of sumatriptan.

Oxford et al. teaches sumatriptan in claim 1, the succinate salt in claim 4, and compositions thereof including pharmaceutically acceptable carriers in claim 5. In

addition, the reference teaches several methods of producing a solid form of sumatriptan product including a method to produce crystalline sumatriptan succinate (line 13 on page 26: example 19). Since the experimental data associated with the product are an intrinsic to it, the anticipation of the product necessarily anticipates any X-ray, DSC, IR, and any other measurements of said product. Claims 10-12 teach the use of the product for the treatment of migraine.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-24, 27-30, 36-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Oxford et al. in view of Brittain ("Polymorphism in Pharmaceutical Solids", V. 95, New York, Marcel Dekker, Inc., 1999) and further in view of Dorsey (John G. Dorsey, "Liquid chromatography", in AccessScience@McGraw-Hill, http://www.accessscience.com, DOI 10.1036/1097-8542.386200, last modified: June 3, 2002) and Vogel ("Practical Organic Chemistry:, 3rd edition, 1966, Wiley, New York).

The claims recite a product referred to as "A crystalline Form" (-I and -II) of sumatriptan succinate, and the intrinsic experimental data including X-ray powder diffraction, differential scanning calorimetry (DSC), and infra red (IR); compositions thereof, the same product at varying degrees of purity, and "A crystalline form of

sumatriptan base" at varying degrees of purity. In addition, the claims are drawn to methods of using the products for treating migraine.

The claims are also drawn to processes of making the aforementioned products including dissolving sumatriptan in an organic solvent, adding succinic acid, inducing crystallization, and isolating the product; the same product at varying degrees of purity, and "A crystalline form of sumatriptan base" at varying degrees of purity.

The claims are also drawn to a process which prepares "highly pure" sumatriptan by dissolving said compound in acetone, treating with charcoal, cooling to 0-30C, and isolating the product to varying degrees of purity using HPLC (high pressure liquid chromatography), 99, 99.5, 99.7, 99.9 % or higher.

The arguable differences in crystal form are clearly taught in by Brittain on page 188-190. Specifically, Brittain teaches methods of producing different forms of pharmaceutical solids by selecting different solvents such as those of table I in combination with different cooling methods and further adjusting the concentrations (see figure 1) and their characterization with X-ray, DSC, and IR. Furthermore, Brittain provides an important motivation for pursuing these different forms on page 184 where these alternate forms may be preferable in instances where absorption of the drug is dissolution rate dependent or may be less susceptible to chemical decomposition which are similar motivations recited in the specification of the instant application.

Dorsey teaches the well-known use of HPLC to purify organic compounds.

Vogel teaches the standard technique of recrystallization of organic compounds from solvents including cyclohexane, acetone, dichloromethane, etc., as well as the use of charcoal for further purification (see pages 125-128).

At the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art to take the products of Oxford et al. and produce various crystal forms including the ones claimed using crystalline polymorph discovery techniques well known in the art and specifically taught by Brittain. As previously discussed, Brittain also provides a motivation to pursue the discovery of alternative crystalline forms of sumatriptan to increase the effectiveness of pharmaceutical solids. Therefore, it would have been obvious to one of ordinary skill in the art to make the claimed products and characterize the intrinsic spectroscopic properties of X-ray, DSC, and IR.

Furthermore, as taught on page 185 of Brittain "It is incumbent on the manufacturer of a new drug substance to show that due diligence has been employed to isolate and characterize the various solid-state forms of a new chemical entity". Thus, there is a reasonable expectation of success that one of ordinary skill in the art would have made the claimed products following the invention of the new chemical entity in Oxford et al. One of ordinary skill in the art would also be motivated by the above statement in Brittain to pursue a product of varying degrees of purity greater than 99% and would have been taught how to achieve this in Dorsey. One of ordinary skill in the art would be also well versed in the techniques of purification by recrystallization

and charcoal taught in Vogel and would have been motivated to make the product as pure as possible since purity ultimately determines the value of an organic compound.

One would be motivated to prepare the instantly claimed invention because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. Since it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism, which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in *In re Cofer* 148 USPQ 268 and *Ex parte Hartop* 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable.

The instant specification and claims claim a known compound, which is the same pure substance as the prior art, only having different arrangements and/or different conformations of the molecule. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis,

hydroscopicity, recovery or prevention of precipitation etc. (see p. 185). Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline form of known compounds would have been suggested to one skilled in the art.

One skilled in the art would have been motivated to prepare different crystalline forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc. Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline forms of known compounds would have been suggested to one skilled in the art.

The compounds are of the same identical formula, the difference, if any, may reside in there being different crystalline forms. One of ordinary skill in the art would be motivated to prepare a different crystalline form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected property (not just a difference in X-ray crystallography), the instant claimed invention is found obvious. The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 13-20, 29, 30, and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, Claims 1-7, 13-20, 29, 30, and 40-42 claim compositions comprising sumatriptan succinate as a solid and pharmaceutical compositions of forms I and II.

The nature of the invention

A solid composition or a pharmaceutical composition comprising Form I and II sumatriptan succinate.

The state of the prior art

The state of the prior art is that the preparation of pharmaceutical compositions requires, milling, adding excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state to resort back to the most thermodynamically stable form which is the form with the lowest vapor pressure. Polymorphs tend to convert from less stable to more stable forms (Brittain, page 184-185). It is also the state of the prior art that an acceptable carrier for a pharmaceutical formulation can be water. Dissolving a specific crystalline form in water, creating an aqueous solution, would put the compound in its free form and not in a crystalline form with a specific X-ray diffraction pattern.

The predictability or lack thereof in the art

The predictability or lack thereof in the art is that a metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern. Also, a solution prepared from a specific crystalline form and water would contain the free form of the compound.

The amount of direction or guidance present and the presence or absence of working examples

While the specification has provided processes for the preparation of the crystalline form I and II, the specification does not provide examples of processes for preparing

pharmaceutical compositions utilizing the crystalline forms I and II. The specification fails to provide the steps of ensuring that the pharmaceutical compositions will maintain the specific forms as found in the specification and will not resort back to the free form or the most thermodynamically stable form of the compound.

The breadth of the claims

A solid composition or a pharmaceutical composition comprising Form I and II sumatriptan succinate.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art, without direction, would be unable to maintain a specific metastable crystalline form upon preparation into a pharmaceutical composition which may require milling or formation of a solution.

The level of the skill in the art

While the level of skill in the art is high, one of skill in the art would be unable to maintain a specific metastable crystalline form upon the preparation of a pharmaceutical composition without direction and guidance which is not found in the instant specification. One of skill in the art would expect the pharmaceutical composition to contain the most thermodynamically stable form of the compound or the free form of the compound.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. The term "highly pure" in claim 8, 12, 24, 27- is a relative term which renders the claim indefinite. The term " highly pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification provides the guidance below, however "at least about 99% pure" is similarly indefinite.

> As used herein, the term "highly pure" means at least about 99% pure by HPLC, more preferably at least about 99.5% pure by HPLC, most preferably at least about 99.7% pure by HPLC.

Conclusion

All claims are rejected.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Cecilia Tsang can be reached at (571)-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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